On the Inter-relations of Genetic Factors.

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The nature and bearing of the observations to be recorded in this paper will best be explained by tracing the steps by which they have been reached.

Early in the investigation of heredity in the sweet pea it was observed that when plants were heterozygous for two separate pairs of allelomorphs the distribution of the factors concerned was in certain cases disturbed in definite ways, such that particular combinations occurred in the gametes with greater frequency than others.

(1) The first case noticed was that of F_1 plants heterozygous for *blue* and *red* colour, and for *long* and *round* pollen. In the F_2 generation all possible combinations were represented, but the blues were for the most part long-pollened and the reds were for the most part round-pollened.

(2) The next case observed was that of F_1 plants heterozygous for *dark* and *light* axils on the one hand, and for *fertile* and *sterile* anthers on the other. In this F_2 also all combinations occurred, but nearly all the dark-axil plants had fertile anthers, while nearly all the light-axilled plants had sterile anthers.

(3) The next step was made by a study of the F_2 from plants heterozygous for *blue* and *red* flowers and for *erect* and *hooded* standards. Here it was found that one of the possible combinations did not exist in F_2, for though the blues might be either erect or hooded, the reds were *all* erect.

Examining these occurrences in the light of the presence-and-absence theory, it was clear that the phenomenon presented by cases (1) and (2) was entirely distinct from that presented by case (3). For whereas in (1) and (2) there was excess of gametes bearing the two factors over those bearing one or the other alone, the condition produced in (3) could only be obtained by a distribution such that no gamete could carry *both* positive factors. We were therefore led to recognise—

A. A system of partial *coupling* under which two factors are generally associated.

B. A system of complete *repulsion* (or as we have sometimes called it, "spurious allelomorphism") under which two factors are never associated in the same gamete.

The partial coupling was next shown to be approximately in case (1)

$$7BL : 1Bl : 1bL : 7bl,$$

where B is blue and L is long pollen ;*

and in case (2) to be

$$15DF : 1Df : 1dF : 15df,$$

where D is dark axil and F is fertile anthers.

(4) At this stage, investigation of the properties of the exceptional members of the F_2 series was begun. In particular, the combination dark axil with sterile anthers (Df) was crossed with a light-axilled plant having normal anthers (dF). The F_2 generation from this cross was, to our surprise, a series in which *all the sterile plants had dark axils.* Here, therefore, there had been a repulsion between the same two factors which had been coupled in case (2).

In considering what could have determined this difference in behaviour, it seemed possible that the distinction might have been due to the way in which the factors had been combined in the original parents, for we knew that in the cases where coupling had resulted, the two dominant factors had been introduced together from the same parent, whereas in this new case one had come from each parent.

For several years this conjecture has been made the subject of elaborate tests, and its correctness has now been completely substantiated in several examples. Expressed in a general form, the conclusion to which we have been led is that if A, a, and B, b, are two allelomorphic pairs subject to coupling and repulsion, the factors A and B will repel each other in the gametogenesis of the double heterozygote resulting from the union

$$Ab \times aB,$$

but will be coupled in the gametogenesis of the double heterozygote resulting from the union

$$AB \times ab.$$

The F_1 heterozygote is ostensibly identical in the two cases, but its offspring reveals the distinction. We have as yet no probable surmise to offer as to the essential nature of this distinction, and all that can yet be said is that in these special cases the distribution of the characters in the heterozygote is affected by the distribution in the original pure parents.

In F_2, from a system in which A and B are coupled, almost all the offspring in the form AaBb will be again built up from AB and ab gametes,

* There are indications that this distribution may be liable to disturbance by other factors in a way not yet understood ('Reports Evol. Committee,' IV, pp. 11—13).

so that they will again exhibit coupling; but a very small proportion will be formed from the comparatively rare gametes aB and Ab. Such heterozygotes will probably show repulsion in their gametogenesis. They must, however, be so rare (only 2 in 256, for example, from the system 7AB : 1aB : 1Ab : 7ab) that it is almost hopeless to look for them in practice.

We know, moreover, that these phenomena are not peculiar to the sweet pea, but that they must exemplify widespread principles of genetic physiology. Repulsion has been found between the factor for femaleness and several factors of various kinds in animals—*e.g.*, in *Abraxas grossulariata*; in the canary; in the fowl for at least three factors—*i.e.* (1) the factor which inhibits the development of the peculiar mesoblastic pigment of the Silky, (2) the dominant " silver " of Assendelvers (Hagedoorn) and of Sebrights (ourselves, unpublished), (3) the barring factor of Plymouth Rocks (Spillman; Pearl). Coupling till recently had been observed in the sweet pea only. Now we have the additional examples published simultaneously with this note, namely, tendrils and round seed in Pisum (de Vilmorin and Bateson), and short style and magenta colour in *Primula sinensis* (Gregory). In addition to these cases of coupling, Gregory also contributes a new example of repulsion, between green stigma and the factor which diminishes the stem-colour. There is thus good reason to believe that these phenomena are of no restricted occurrence in nature.

In work already published we have shown that coupling occurs according to the systems

$$7AB : 1aB : 1Ab : 7 ab$$

and
$$15AB : 1aB : 1Ab : 15ab.$$

Such systems pointed to the existence of others which could be given by the expression

$$3n^2 - (2n-1) : 2n-1 : 2n-1 : n^2 - (2n-1),$$

where n is half the number of gametes needed to express the whole system.

Two more of the systems thus contemplated as possibilities have been discovered. The cases now stand thus:—

3 : 1. No case yet known.

7 : 1. *Sweet Pea.* Blue factor and long pollen.

7 : 1. *Primula sinensis.* Magenta colour and short style.

15 : 1. *Sweet Pea.* Fertile anthers and dark axils.

31 : 1. No case yet known.

63 : 1. *Pisum.* Development of tendrils and round seed.

127 : 1. *Sweet Pea.* Blue factor and erect standard.

For all of these except the Pisum case (as yet untried) repulsion is also

proved to occur.   We know also that repulsion occurs between long pollen and the erect standard in families where blues are not present, but hitherto we have not had an opportunity of determining the system of coupling followed by this pair of factors.

Several curious and important lines of inquiry are thus opened up.   As to the actual meaning or nature of coupling or repulsion there is no clue. The fact, however, that the mode in which factors are combined in the original parents can influence the distribution of the factors among the gametes of F_1 introduces a new conception into genetic physiology. Reciprocal matings give identical results, so no mere question of maternal influence is involved.

In attempting to form any conception of what actually happens in coupling or repulsion, and of the cause which determines that the one phenomenon or the other shall occur, we are met at once by the difficulty that we do not yet know how or when the system $1\,AB : 1\,aB : 1\,Ab : 1\,ab$, which we regard as the normal distribution for two pairs of allelomorphs, is produced. There is as yet no proof that the segregation of both pairs of factors occurs at one division, or that that division is one of those which we regard as specially concerned in maturation.   Now that we know of a series involving as many as 256 terms $(127 + 1 + 1 + 127)$ it is most difficult to conceive that such a system can be produced in the maturation-divisions of the ovarian tissue of such a plant as a sweet pea.   We may well be tempted to look much earlier in the developmental processes for the establishment of these differentiations, and it is not impossible that they may be established as early as the embryonic constitution of the sub-epidermal layer itself.   As is known, this layer is—in most higher plants, at least—the exclusive source of the germ-cells, a fact which leads to those remarkable consequences which Baur has discovered in the genetics of variegated plants.   Remote as this possibility admittedly is, in a problem of such extreme difficulty even improbable suggestions are worthy of consideration.

If we knew how the normal distribution, $1\,AB$, $1\,aB$, $1\,Ab$, $1\,ab$, is brought about we might surmise by what modification the other distributions are created.   As it is, we can only say that in repulsion the heterozygote AaBb gives off germ-cells of two types, Ab and aB, whereas in a coupled system there are four types, AB, Ab, aB, ab, the two terms AB and ab being represented 7 times, 15 times, etc.   One step further may perhaps be gained by arranging the symbols so as to represent the combinations more accurately to the eye—

$$1. \quad Ab \times aB. \qquad\qquad 2. \quad AB \times ab.$$
$$Ab \,.\, aB. \qquad\qquad\qquad AB \,.\, ab.$$

The heterozygote Ab.aB forms only two types of gametes, and the heterozygote AB.ab gives the coupled series of four types.   Since the same factors are involved in both cases it looks possible that the difference in behaviour may be a consequence of the difference in the geometrical positions of the factors relative to the planes of some critical division or divisions in the two cases.   There may, in fact, be a difference of polarity between the two kinds of heterozygote.

The increase in number of the two types of cell, AB and ab, may be reached by proliferation of the two primordial cells of those two types.   It may further be remarked that though the numbers characteristic of coupled systems cannot be produced by simple dichotomies, they can readily be represented as produced by a series of periclinal and anticlinal divisions.   For example if AB^1 by periclinal division give off AB^2, and this by anticlinal division become two cells, which again divide periclinally and anticlinally, seven cells AB are formed; by repetition of the same processes 15 are formed, and so on.

Systems of three Factors.—From the list given above it will be seen that in the sweet pea we know two distinct factors, viz., erect standard and long pollen, which may be severally coupled with a third factor, that for blue colour.   Here, therefore, we meet a system of inter-relationship between *three* pairs, and special interest must attach to a determination of the genetic properties of plants heterozygous for all three. (The distribution of the factors for fertile anthers and dark axils, so far as evidence goes, is independent of this system of three pairs, so that, for the present, fertility of anthers and axil-colour can be left out of account in a consideration of the triple system.)

A plant heterozygous for B (blue), L (long pollen), and E (erect standard), can be made by any of four possible combinations.

(1) EBL × ebl.

(2) EBl × ebL.

(3) Ebl × eBL.

(4) eBl × EbL.

All these various types of combinations are now either made or being made, but as yet we are only able to give the result in the case of No. 3. In it B and E repel, and B is coupled with L on the 7:1 system.   The coupling of B with L, since they come in together, may seem to be what the general trend of the evidence leads us to expect, but the fact that E is repelled by B rather than by L is worthy of special notice, for we know that E and L repel each other when B is not present.   It suggests

that there must be an "order of precedence" among the factors composing such a system, and the suggestion is plausible that this order will follow the grade of coupling in which the factors are accustomed to be linked.

It will be observed that, given a system under which a pair of factors are coupled, it is possible to produce the system under which the same pair repel each other. For all that is necessary is to breed together the rarer terms of the coupled series, viz., Ab and aB.

From the repelling system, on the contrary, in the absence of a fresh variation, we have no obvious way of constructing the coupled system. This consideration has an obvious application to those cases in which *sex* operates as a repelling factor. In the fowl, the canary, and *Abraxas grossulariata*, femaleness thus acts as a repelling factor against various elements determining pigmentation ; and our experience of the plants leads us to suppose that if the factors involved could be built up in the right combinations, femaleness might be coupled with the factors it now repels.

Extraordinary consequences, both to the distribution of the sexes, to the distribution of factors between them, and perhaps to the causation of fertility, must be anticipated if this condition could be fulfilled. There may be an indirect way of actually accomplishing these results. For, seeing that sex in the fowl acts as a repeller of at least three other factors, when birds are built up so as to be heterozygous for several of these, some of them may be found able to take precedence of the others in such a way as to annul the present repulsions, with subsequent coupling as a consequence.